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Demonstration of the "No-Reflow" Phenomenon by Digital Coronary Arteriography

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Incomplete return of normal blood flow in the reperfusion period after prolonged ischemia has been termed the "no-reflow" phenomenon.¹ This has only recently been demonstrated in humans by intracoronary thallium-201 scintigraphy.² In this report, we demonstrate the "no-reflow" phenomenon in a patient by digital coronary arteriography.

A previously healthy 58-year-old woman with 3 hours of anginal chest pain associated with precordial ST-segment elevation was treated with 1.5 million U of intravenous streptokinase. Cardiac catheterization was performed 5 hours after the onset of symptoms. Coronary arteriography showed widely patent coronary arteries. The left ventricular ejection fraction was 39%, with regional akinesia in the distribution of the left anterior descending coronary artery (Fig. 1). The hospital course was unremarkable. Peak creatine kinase level was 849 IU. Repeat cardiac catheteriza-

tion was done 9 days later. The left ventricular ejection fraction was 58%, with apical akinesia (Fig. 1). Coronary arteriographic findings were again normal, and ergonovine (0.3 mg) provocation was negative. Uncertain whether the myocardial infarction was a

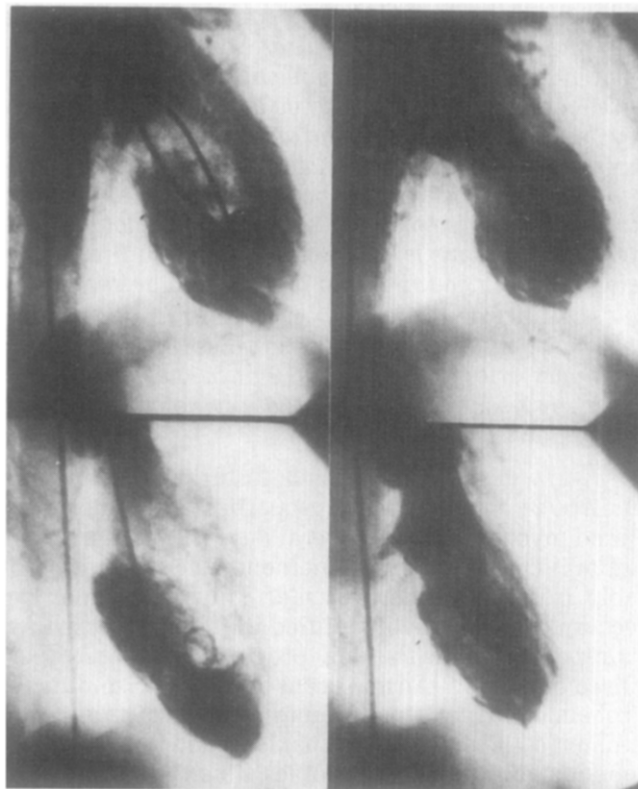


FIGURE 1. Left ventriculograms in the right anterior oblique projections immediately after intervention (top) and 9 days later (bottom). End-diastolic (left) and end-systolic (right) frames are shown. Left ventricular function is markedly improved at the second study.

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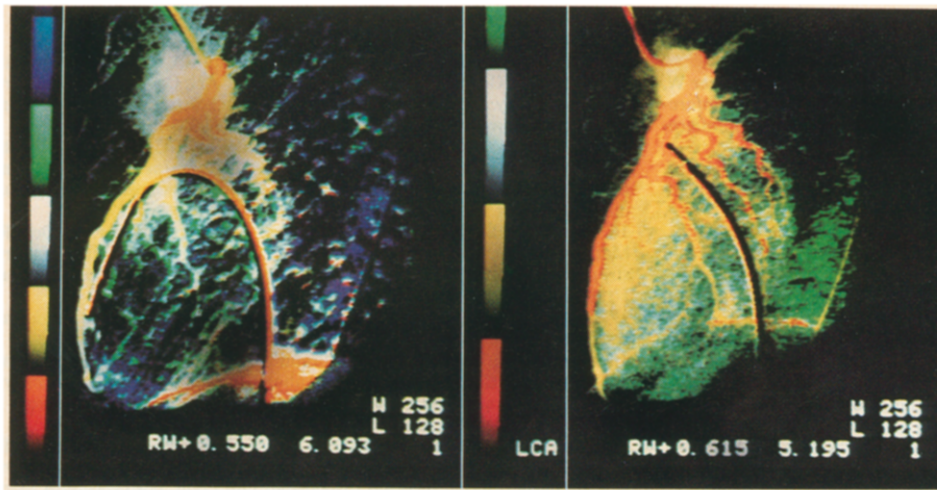


FIGURE 2. Contrast medium appearance pictures of the left coronary artery in the left anterior oblique projection acutely after intervention (*left*) and 9 days later (*right*), with a 3.6-fold increase in relative regional blood flow in the left anterior descending perfusion bed.

result of coronary emboli or spasm, we empirically treated the patient for both with chronic aspirin, dipyridamole and diltiazem therapy.

Digital coronary arteriography of the left coronary artery was performed during both catheterization procedures.³ Contrast medium was power injected and synchronized to the R wave of the electrocardiogram at a rate of 4 ml/s for a total of 7 ml. One gated end-diastolic image per cardiac cycle was acquired. Pictures of contrast medium appearance were then generated by mask mode subtraction (Fig. 2). The intensity of each pixel corresponds to the maximal contrast density reached during each acquisition, while the appearance time of contrast in the pixel is color-modulated, with a different color assigned to each post-contrast injection cardiac cycle (red for the first cycle, yellow for the second, and so on). Because contrast density is directly related to volume of distribution in the myocardium and flow is inversely related to appearance time, digital estimation of relative coronary blood flow is calculated as the contrast density/appearance time ratio in a defined area of interest. During the acute study, the contrast density/appearance time ratio for the left anterior descending coronary artery was 0.07 and 9 days later, it was 0.25. This represents 3.6-fold increase in relative regional blood flow.

A few minutes of ischemia disturbs the structural, metabolic and functional properties of reversibly injured myocardium for several days (stunned myocardium).⁴ The no-reflow phenomenon, however, is probably caused by microvascular injury and does not occur until irreversibly injured ischemic myocardium is reperfused.⁵ In the dog, progressive loss of reperfused blood flow starts to occur only after 25 minutes of ischemia, but is virtually complete after 60 minutes of ischemia.⁶ Postulated mechanisms for the no-reflow phenomenon include endothelial cell swelling, perivascular edema, capillary plugging by erythrocytes or leukocytes, and small vessel spasm.^{1,7}

In the report by Schoffer et al,² the acute residual thallium-201 defect representative of the no-reflow phenomenon was unchanged 2 to 4 weeks after thrombolysis. The contrast medium appearance picture gen-

erated by our digital technique, however, demonstrated a diffuse decrease in regional flow, which improved 9 days after infarction. These discordant findings are probably reconciled by recent data published by Kloner and Alker⁷ in a dog model. They describe areas of very low myocardial blood flow after reperfusion associated with anatomic perfusion defects, microvascular damage, and infarcted tissue consistent with no reflow. In addition, however, areas of low reflow detected by microspheres were present in the ischemic subepicardium, which did not have microvascular damage or anatomic perfusion defects. They postulated that low reflow was a result of the lower oxygen demand of the stunned myocardium.

The marked improvement in ventricular function and the low creatine kinase level in our patient suggest early reperfusion, a limited apical infarction, and a large area of stunned myocardium which recovered normal function. Flow data from our digital radiographic technique during reperfusion are probably more consistent with microsphere flow data showing reduced flow than with thallium-201 perfusion data, which reflect only lowest flow owing to myocardial infarction. Application of digital and scintigraphic techniques should allow further investigation of stunned myocardium and the no-reflow phenomenon in humans.

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